

Supplementary Table 1. Human studies addressing the effects of nutrition in Parkinson's disease.

E represents an epidemiological study and R represents a review.

Classification	Study Results	References
Dairy	<p><u>Dairy Constituents</u> Dairy fat, protein and lactose increases risk of PD.</p> <p>Dairy consumption may increase the risk of PD, particularly in men.</p> <p>E (Saaksjarvi et al., 2013)</p> <p>Lack of association between dairy products and risk of PD.</p> <p>High consumption of dairy results in low urate levels.</p> <p>High plasma levels of uric acid may modify the risk of PD.</p> <p><u>Calcium</u> Calcium and vitamin D are positively associated with PD risk only when derived from dairy products.</p> <p><u>Vitamin D</u> High consumption of food containing vitamin D increases risk of PD in humans.</p>	<p>E (Hellenbrand et al., 1996b;Chen et al., 2002;Park et al., 2005;Chen et al., 2007a;Kyrozis et al., 2013)</p> <p>E (Chen et al., 2007a)</p> <p>Milk consumption is positively associated with PD risk in women. E (Miyake et al., 2011c)</p> <p>E (Choi et al., 2005a)</p> <p>R (Schlesinger and Schlesinger, 2008)</p> <p>E (Chen et al., 2002)</p> <p>E (Anderson et al., 1999)</p>
Fat	<p><u>Fat</u> A higher risk of PD is seen with greater intake of total fat- saturated and animal.</p> <p>No association between PD and fat intake was observed.</p> <p>A ketogenic diet provides symptomatic and disease-modifying activity in PD.</p> <p><u>A modified ketogenic diet consisting of mono and polyunsaturated fats improved the Unified Parkinson's Disease Rating Scale.</u></p> <p>Intake of PUFAs is protective for PD as well as MUFAs.</p>	<p>E (Logroscino et al., 1996;Anderson et al., 1999;Chen et al., 2003)</p> <p>E (Hellenbrand et al., 1996b;Logroscino et al., 1996;Johnson et al., 1999;Chen et al., 2002;Powers et al., 2003)</p> <p>R (Gasior et al., 2006)</p> <p>E (Vanitallie et al., 2005)</p> <p>E (Abbott et al., 2003;de Lau et al., 2005)</p>

	<p><u>Polyunsaturated fatty acids</u> PD patients exhibit higher concentrations of PUFA peroxidation metabolites, but lower concentrations of PUFA and glutathione in the SN compared to controls.</p> <p>PUFAs intake is associated with lower PD risk.</p> <p><u>Cholesterol</u> An association between cholesterol and PD is highly debated. Lower plasma cholesterol concentrations and biosynthesis is found in PD patients compared to controls and that statins use may lower PD occurrence.</p> <p>Increased cholesterol levels are associated with lower PD risk, primarily in women.</p> <p>Higher total serum cholesterol may be associated with a modest slower progression of PD.</p> <p>Total HDL-cholesterol ratio is inversely associated with duration of PD and may contribute to cardiometabolic protection.</p>	<p>E (Chen et al., 2003)</p> <p>E (Kamel et al., 2013)</p> <p>R (Hu, 2010)</p> <p>E (Lamperti, 1991)</p> <p>E (de Lau et al., 2006)</p> <p>E (Huang et al., 2011)</p> <p>E (Cassani et al., 2013)</p>
Fruits and Vegetables	<p>Nicotine-containing vegetables from edible Solanaceae are associated with a reduced risk of PD.</p> <p>A dietary pattern including high consumption of fruits, vegetables and fish are inversely associated with PD risk.</p> <p>No relationship was found between intake of vegetables or fruit and the risk of PD.</p> <p><u>Vitamin C</u> Higher intake of fruits and certain vegetables containing vitamin C is associated with an increased risk of PD.</p> <p>No significant association between vitamin C from food and PD.</p> <p><u>Vitamin E</u> Vitamin E from food is associated with a lower risk of PD, particularly in men.</p>	<p>E (Searles Nielsen et al., 2013)</p> <p>E (Gao et al., 2007; Okubo et al., 2012)</p> <p>E (Miyake et al., 2011a)</p> <p>E (Scheider et al., 1997)</p> <p>E (Zhang et al., 2002; Etminan et al., 2005)</p> <p>E (Zhang et al., 2002)</p>

<p>Carbohydrates</p>	<p>High glycemic index foods decrease the risk of PD.</p> <p>Carbohydrate consumption and PD risk is reported with a non-significant direct association in women and inverse association in men.</p> <p>Total carbohydrate consumption is positively associated with PD.</p>	<p>E (Murakami et al., 2010a)</p> <p>E (Chen et al., 2003)</p> <p>E (Hellenbrand et al., 1996a)</p>
<p>Protein</p>	<p><u>Protein</u> No correlation is found with total protein intake and the risk of PD.</p> <p>Elimination of dietary red meat accompanied with high doses of riboflavin promotes recovery of motor functions in PD patients.</p>	<p>E (Hellenbrand et al., 1996b; Logroscino et al., 1996; Johnson et al., 1999; Chen et al., 2003)</p> <p>E (Coimbra and Junqueira, 2003)</p>
<p>Beverages</p>	<p><u>Caffeine</u> Caffeinated beverages may provide neuroprotection against PD.</p> <p>Coffee drinking in women who are not taking hormone-replacement therapy is associated with a reduced risk in PD as observed in men.</p> <p>Clinical studies are underway to evaluate several A_{2A} receptor antagonists for symptomatic relief and slowing of disease progression in PD.</p> <p>Caffeine appears to improve motor and non-motor conditions in PD clinical trials. Gastrointestinal discomfort and anxiety were common adverse effects.</p> <p><u>Tea</u> Black tea drinking shows an inverse association with PD risk whereas green tea was unrelated to PD risk in a Chinese population.</p> <p>Tea consumption may reduce the risk of PD.</p> <p>Tea consumption delayed onset of motor symptoms in PD patients.</p> <p><u>Alcohol</u> No association between alcohol consumption and PD.</p>	<p>R (Prakash and Tan, 2011)</p> <p>E (Ascherio and Chen, 2003; Palacios et al., 2012a)</p> <p>R (Barkhoudarian and Schwarzschild, 2011; Hickey and Stacy, 2011)</p> <p>E (Altman et al., 2011)</p> <p>E (Tan et al., 2008)</p> <p>E (Chan et al., 1998; Checkoway et al., 2002)</p> <p>E (Kandinov et al., 2009)</p> <p>E (Benedetti et al., 2000; Checkoway et al., 2002; Hernan et al., 2003; Palacios et al., 2012b)</p>

	<p>Inverse association between alcohol consumption and PD.</p> <p>Low to moderate beer consumption may lower the risk of PD whereas high liquor consumption may increase PD risk.</p>	<p>E (Ragonese et al., 2003)</p> <p>E (Liu et al., 2013)</p>
Supplements	<p><u>Beta-carotenoids</u> Higher intake of beta-carotenoids is associated with a decreased risk of PD in women.</p> <p><u>Vitamin B - Riboflavin</u> Daily doses of riboflavin for 6 months show improved motor capacity in PD patients in 3 months.</p> <p>Riboflavin is not associated with risk of PD.</p> <p>Low intake of vitamin B6 is associated with an increased risk of PD.</p> <p>Folate, vitamin B6 and B12 are not associated with a risk of PD.</p> <p><u>Vitamin C</u> Vitamin C is not associated with PD risk.</p> <p><u>Vitamin D</u> Intake of vitamin D is not associated with PD risk.</p> <p>Vitamin D3 supplementation prevented the deterioration of the Hoehn & Yahr stage in PD patients compared to placebo-controlled group.</p> <p><u>Vitamin E</u> Vitamin E is not associated with PD risk.</p> <p>Clinical trials show no neuroprotective benefit of taking vitamin E.</p> <p>Higher intake of vitamin E is associated with a reduced risk of PD in women.</p>	<p>E (Miyake et al., 2011a)</p> <p>E (Coimbra and Junqueira, 2003)</p> <p>E (Abbott et al., 2003; Murakami et al., 2010b)</p> <p>E (Murakami et al., 2010b)</p> <p>E (Chen et al., 2004)</p> <p>E (Zhang et al., 2002) E (Miyake et al., 2011a)</p> <p>E (Chen et al., 2002)</p> <p>E (Suzuki et al., 2013)</p> <p>E (Zhang et al., 2002)</p> <p>E (Fernandez-Calle et al., 1992; LeWitt, 1994)</p> <p>E (Miyake et al., 2011a)</p>

Supplementary Table 2. Animal and *in vitro* studies addressing the effects of nutrients in Parkinson's disease. A is animal and IV is *in vitro*.

Classification	Study Result	Reference
Fat	A high fat diet exacerbates the progression of PD in rodents by increasing DA depletion and damage.	A (Choi et al., 2005b; Morris et al., 2010; Bousquet et al., 2011b)
	Polyunsaturated fatty acids inhibit neuronal apoptosis in cellular models.	IV (Kim et al., 2001)
Docosahexaenoic acid (DHA)	DHA reduces apoptosis in dopaminergic cells and preserves DA levels from MPTP-induced neurotoxicity in mice.	IV (Ozsoy et al., 2011) A (Bousquet et al., 2008)
	DHA protected neurons against cytotoxicity, inhibition of NO production, Ca^{2+} influx, and increased the activities of antioxidant enzymes glutathione peroxidase and glutathione reductase.	A (Wang et al., 2003)
	Short-term administration of DHA reduced levodopa-induced dyskinesias in Parkinsonian primates.	A (Samadi et al., 2006)
	DHA treatment elevated DA levels in a 6-OHDA model of PD.	A (Cansev et al., 2008)
	DHA supplementation replaces omega-6-PUFAs already present in the brains post-MPTP treatment.	A (Bousquet et al., 2008)
Eicosapentaenoic acid (EPA)	EPA attenuated motor impairments, and inflammation in a MPTP model of PD.	A (Luchtman et al., 2012) IV (Luchtman et al., 2013)
Caffeine	Chronic caffeine administration in mice provided protection against dopaminergic neuron toxicity from exposure to a combination of common pesticides- Paraquat and Maneb.	A (Kachroo et al., 2010; Yadav et al., 2012)
	Acute and chronic caffeine administration reduced the effect of acute MPTP and 6-OHDA treatment on striatal DA loss.	A (Chen et al., 2001; Joghataie et al., 2004)
	Caffeine treatment partially restored DA and its metabolites in 6-OHDA-lesioned rats.	A (Aguiar et al., 2006)
	Caffeine is neuroprotective in MPTP model of PD.	A (Xu et al., 2010)

	<p>Chronic caffeine treatment prevented DA cell degeneration in a MPTP model of PD. Neuroprotection was still observed after the onset of PD.</p> <p>Caffeine reduces neurotoxicity through antagonism of adenosine A_{2A} receptors.</p> <p>Methylxanthine A_{2A} receptor antagonists may cause oxidative stress in PD.</p>	<p>A (Sonsalla et al., 2012)</p> <p>R (Morelli et al., 2010; Prediger, 2010)</p> <p>A (Golembiowska and Dziubina, 2012)</p>
Soy	<p>Pre-treatment of parkinsonian rats with dietary soy meal improved spatial learning and memory.</p> <p>Genistein appears to be neuroprotective in ovariectomized rats, thereby suggesting it may be useful for prevention of PD in post-menopausal women.</p> <p>Genistein protects dopaminergic neurons from lipopolysaccharide-induced injury.</p> <p>Pre-treatment with genistein restored MPTP-induced down regulation of TH, dopamine transporter and Bcl-2 mRNA expression in the midbrain.</p> <p>Genistein administration attenuated the rotational behavior in lesioned rats and protected neurons against 6-OHDA toxicity.</p>	<p>A (Sarkaki et al., 2009)</p> <p>A (Kyuhou, 2008)</p> <p>IV (Wang et al., 2005)</p> <p>A (Liu et al., 2008)</p> <p>A (Baluchnejadmojarad et al., 2009)</p>
Polyphenols	<p><u>EGCG</u> The green tea polyphenol EGCG is neuroprotective by preventing neurotoxin-induced cell injury and prevent MPTP-induced dopaminergic neurodegeneration.</p> <p>EGCG provides neuroprotection through nitric oxide reduction.</p> <p>Oral treatment with EGCG provided symptomatic relief but no neuroprotection in 6-OHDA model of PD.</p> <p><u>Quercetin</u> Quercetin prevents apoptosis of DA-producing neurons.</p> <p><u>Resveratrol</u> Resveratrol reduces deterioration caused by free radicals preventing subsequent behavioral, biochemical, and histopathological changes that</p>	<p>R (Mandel et al., 2004) A (Levites et al., 2001)</p> <p>A (Kim et al., 2010)</p> <p>A (Leaver et al., 2009)</p> <p>IV (Bureau et al., 2008)</p> <p>IV (Bureau et al., 2008)</p>

	<p>occur during PD.</p> <p>Resveratrol prevents apoptosis of DA-producing neurons and exerts neuroprotective effects on 6-OHDA-induced animals by reducing inflammatory reactions as well scavenging free radicals in MPTP.</p> <p>Theaflavin mediated neuroprotection in MPTP model of PD.</p> <p><u>Carotenoids</u> Pretreatment with beta-carotene partially protected against MPTP-induced neurotoxicity in mice, but not in primates.</p> <p>Lycopene reduces oxidative stress and cognitive decline in a rotenone induced model of PD.</p> <p><u>Sulforaphane</u> Ameliorated motor deficits prevented dopaminergic cell death by modulating oxidative stress.</p> <p><u>Erucin</u> Treatment with erucin provided neuroprotective effects against 6-OHDA in a neuronal cell culture model.</p>	<p>A (Blanchet et al., 2008;Jin et al., 2008;Lu et al., 2008)</p> <p>A (Anandhan et al., 2012)</p> <p>A (Perry et al., 1985;Perry et al., 1987)</p> <p>A (Kaur et al., 2011)</p> <p>A (Morrioni et al., 2013)</p> <p>IV (Tarozzi et al., 2012)</p>
Wheat germ	Wheat germ oil is neuroprotective in 6-OHDA model of PD.	A (Wang et al., 2010)
Vitamin D	Vitamin D is beneficial in animal and cell culture models of PD.	A (Wang et al., 2001;Smith et al., 2006) IV (Holick, 2007)
Vitamin E	Vitamin E supplementation protected DA neurons in the SNpc, reduced DA loss and showed protection against paraquat toxicity.	A (Lan and Jiang, 1997;Storch et al., 2000a;Roghani and Behzadi, 2001)
Curcumin and naringen	Curcumin and naringenin promote neuroprotection in PD.	IV (Chen et al., 2006) A (Zbarsky et al., 2005;Rajeswari, 2006)

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References

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